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ell elmelmaa, ludilla Modelitest, Joseph Nation, Amand larm, Isen Hamming, Jester l-ach, lana Mielsen, Klaus Karlsson, Gunilla Rasmussen, Peter



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<131> 3631-0109P

4140 / US 09/806,103

<1412 2001-04-04

<150> POT/DK99/00525

<151> 1999-10-05

<150> DK 1998 01261

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Leu Lys Ser Pro Asp Glu Gly Phe Glu Gly Lys Ser Leu Tyr Glu Ser
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<pre>cig dgi Led Sly <210> 4 <211> 1 <212> 6 <413> 8 <4130 4</pre>	1.6û 288 RT calo :	Asp.	ing Nai	oda Pro	Val		~~r	27 4-	F 2015	ī.ac	· An	Al a	*an	i.an	3768
<pre>cig dg Led Gly <210> 4 <211> 1 <212> F <401> E <400> 4 Met Glu</pre>	188 RT Check	Asp Ala Hul	Tal Tal 1230	eca Pro Leu	Val.	Arg	-15					- 1 .			376 3
<pre>cig gg Led Gly <2105 4 <2115 1 <2125 E <4005 4 Met Gld Pro Pro Pro Pro</pre>	Led 255 RT cmc : Led 317	Adpik Ala Huli Ala	Nal Val 1430 Ala Ala	cca Pro Leu Ser	Vai Cys Thr	Arg Sin	-15 Val	Tys	Thr	Gly S	Thr	-1.1 Asy	Ma*	178	3768
<pre>cig gg Led Gly <210> 4 <211> 1 <212> F <401> 4 Met Glu Pro Pro Led Ar: 10</pre>	Lea Lea Jea	Ada Ala -Ul Ala Pro	Stg Val 1230 Ala Ala	Ecca Pro	Cys Thr Fro	Arg Sin Tu	-15 VA:	Tys His	Thr Leu 20	Gly 5 Asp	Thr	-10 Asp Leu	Met Ard	Lys His	3768
<pre>cig gg Leu Sly <210> 4 <211> 1 <212> E <4113> E <4113> E <4113> E cut Slu Pro Pro Leu Arr 112 Leu Tyr </pre>	Lea Strong of Lea Jea Jea Jea Jea Jea	Asp Ala Hul Ala Pro	Star Value Alla Alla Cys	Dea Pro	Cys Thr Fr:	Arg Sin i tlu Val	-18 Val Thr Gl:	Tys His	Thr Leu 20 Asn	Gly S Asp Leu	Thr Met	HID Asp Leu Leu	Met Ard Thr	Lys His Lis Tyr	3768
<pre>cig dar Leu Sly <210> 4 <210> 6 <211> 1 <212> 6 <4013> H <4013> H Met Glu Pro Pro Leu Arr 10 Leu Typ Leu Typ Leu Fr</pre>	Led Stockers Led Sty The a	Asp. sapis Ala Hro Gly Asp. 45	Cys. Ala Cys. Ala	De la	Cys Thr -1 Pro Val	Arg Sin Tal Val	-18 Val Thr Sin	Cys His Ty Ten	Thr Leu 20 Ash Vin	Gly E Asp Leu Asy	Thr Met Sla	HID Ask Lett	Mer Ard Thr	Lys His Lit Tyr	3768
<pre>cig dar Leu Cly <210> 4 <210> 6 <211> 1 <411> E <411> E <411> E <4110</pre>	Led Stockers Led Sty Tes This	Ada Ala Ala Pro Gly Ada Udi	Ala Ala Cyso Ala Lou	Dominion of the second of the	Cys Thr Fro Val Loca Alla	Arg Sin Tiu Val Ser	-18 Val Thr Gli Pho Aun	Cys His Hy His His His His His	Thr Leu 20 Ash Whi	Gly 8 Asp Led Asp	Thr Met 31d 114	Led Led Led Led Unit	Mer Ard Thr idea	Lys His 105 Tyr Val	3768
<pre>cig dar Leu Sly <210> 4 <210> 6 <211> 1 <212> 6 <4013> H <4013> H Met Glu Pro Pro Leu Arr 10 Leu Typ Leu Typ Leu Fr</pre>	Led Stockers Led Sty Tes This	Ada Ala Ala Pro Gly Ada Udi	Ala Ala Cyso Ala Lou	Dominion of the second of the	Cys Thr Fro Val Loca Alla	Arg Sin Tiu Val Ser	-18 Val Thr Gli Pho Aun	Cys His Hy His His His His His	Thr Leu 20 Ash Whi	Gly 8 Asp Led Asp	Thr Met 31d 114	Led Led Led Led Unit	Mer Ard Thr idea	Lys His 105 Tyr Val	3768
<pre>cig dar Leu Cly <210> 4 <210> 6 <211> 1 <411> E <411> E <411> E <4110</pre>	Led Sassano Led Sano Led Sano Sano Sano Sano Sano Sano Sano Sano	Ada Ala Ala Pro Gly Ada Val	Star Val Mala Ala Ala Ala Vys Ala Deu	Le se	Cys Thr Fro Val Loca Acces Acces	Arg sin : tiu Val Val : His . i	H15 Val Thr Sin She Ash	Tys His Tyy Ten Th	Thr Leu 20 Ash Win Wil	Gly E Asp Led Asy Art	Thr Met Alm illa illa illa illa	Asp Lett Lett Sind Type Ads	Met Arus Thr is the Arus Arus Arus Arus Arus Arus	Lys His Lis Tyr Vai Lya	3768
<pre>cig dg Led Gly <210> 4 <211> 1 <211> 1 <211> 2 <411> 4 <411> 4 Met Glu Pro Ero Led Typ Led Typ Led Typ 10</pre>	Led Sassano Led Sano Led Sano Sano Sano Sano Sano Sano Sano Sano	Ada Ala Ala Pro Gly Ada Val	Star Val Mala Ala Ala Ala Vys Ala Deu	Le se	Cys Thr Fro Val Loca Acces Acces	Arg sin : tiu Val Val : His . i	H15 Val Thr Sin She Ash	Tys His Tyy Ten Th	Thr Leu 20 Ash Win Wil	Gly E Asp Led Asy Art	Thr Met Alm illa illa illa illa	Asp Lett Lett Sind Type Ads	Met Arus Thr is the Arus Arus Arus Arus Arus Arus	Lys His Lis Tyr Vai Lya	3768

that the sty Alack materially stylic, because the Lea Arabit a inn A. Isabe, iya ay ay sacasa sa An Ang Am Fr iya iya kun Azşı inn The Lew Ing Ty Day The Bha His Lyo A : The Levy Ala Levy Thr Levy 112 Agr (for Ash Arg Ser Ar) Ala ::<u>⊕</u>• Dys Dys dly Jer Arri Bin Wer Lea Thr Ard inc Ala Ari Oys Lys Gly Fro Leu Pro Thi Asi Tys Cys His Glu Glio Ala Ala Gly Cys Thr Gly Pro Lys His der Asp Cys Leu Ala Cys Leu 2.45 His the Ash His Ser Gly Ile Cys Glu La: His Cys Pro Ala Leu Val 240 Thr Tyr Ash Thr Asp Thr Phe Giu Ser Met Fro Ash Pro Glu Gly Arg Tyr Thr Fhe Gly Ala Ser Cys Val Thr Ala Tys Fro Tyr Asm Tyr Leu Thr Asp Val Gly Ser Cys Thr Leu Val Cys Ero Leu His Asn Gln 285 290 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Tys Glu Lys Cys Ser Lys 300 305 310 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu 320 325 Val Arg Ala Val Thr Ser Ala Ash Ile 31: "The Fhe Ala Gly Cys Lys 335 1.1 Lys Ile Fhe Gly Ser Leu Ala Phe Leu Fr. Hu Ser Phe Asp Gly Asp 350 360 Fro Ala Ser Ash Thr Ala Fro Leu Gl. Fr. Hlu Gln Leu Gln Val Fho 365 Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro 390 385 Asp Ser Leu Pro Asp Leu Ser Val Phe Gin Asn Leu Gln Val Ile Arg २३≓ Bly Arg lle Leu His Ash Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu - - - - -The Sar Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gl; Led Ala Led Ile His His Ash Thr His Let Tys Phe Val His Thr Val Pro Trp Asp 3in Leu Fhe Arg Ash Fr His Win Ala Leu Leu His Th: 460 40€ Ala Ash Ang Pro Glu Asp Glu Cys Val. Tly Tlu Gly Leu Ala Cys His 450 Bin Leu Cys Ala Arg Gly His Cys Trp Bly Fro Gly Pro Thr Gln Cys Val Ash Dys Ser Alm the Leu Ard Aly Alm Alu Dys Val Alu Blu Ard Mal Dog Him Hly Den Fro Ard Him Tyr Mal Ash Ala Ard His Tys His Er - And Tys Bln Er - An Ann Ely Der Wal Thro Encoding the CAIN All Amporting Tym Die Alle Tym Alle Him Tym Lym All

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Glu lle Phe Lys Thr Ser Leu Ser Glu Gln Pro Pro Pro Gly Tyr Glu
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Asm The Ser Asp Val Val Fro Pro Tyr Ser Ala Fhe der Fro Glm Gly
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 Thr Ero Glu Gly Asp Leu Val Tyr Val Asn Tyr Ala Arg Thr Glu Asp
 Phe The Lys Leu Glu Arg Glu Met Lys Ile Ser Cys Ser Gly Lys Ile
                                                        135
        The Ala Arg Tyr Gly Lys Val Phe Arg Gly Ash Met Val Lys Ash
                                              150
                                                                                            155
Ala Gln Leu Ala Gly Ala Lys Gly Met Ile Leu Tyr Ser Asp Pro Ala
                                                                                  170
                                   165
Asp Tyr Phe Val Pro Ala Val Lys Ser Tyr Pro Asp Bly Trp Ash Leu
                                                                          195
 Pro Ply Bly Gly Mal Gln Ard Gly Ash Mal Leu Ash Leu Ash Gly Ala
                   195
                                                                 200
 Gly Asp Pro Leu Thr Pro Gly Tyr Pro Ala Ash Glu His Ala Tyr Arg
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 Wall sly Fro Gly Fhe Ala Gly Ash Phe Ser Thr Nin Lys Wal Lys Mot
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Phe Glu Leu Ala Ash Ser Ile Val Leu Erc Phe Asp Cys Gln Ver Tyr
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Ala Val Ala Leo Lys Lys Tyr Ala Asp Thr Ile Tyr Asm Ile Ser Met
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Lys His Fre Gln Glu Met Lys Ala Tyr Met Ile Ser Phe Asp Ser Leu
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Phe Ser Ala Val Ash Ash Phe Thr Asp Val Ala Ser Lys Phe Ash Gin
Arg Lea Glin Gliu Lea Asp Lys der Ash Pro Ile Leu Lea Arg Ile Met
Ash Asp Gin Leu Met Tyr Leu Glu Arg Ala Phe Tie Asp Pro Leu Gly
                        615
                                            620
Leu Pro Gly Arg Pro Phe Tyr Arg His Thr Ile Tyr Ala Pro Ser Ser
                    630
                                         635
His Ash Lys Tyr Ala Gly Glu Ser Fhe Pro Gly Ile Tyr Asp Ala Leu
               645
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Phe Asp lie Ser Ser Lys Mal Ash Ala Ser Lys Ala Trp Ash Glu Mal
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Lys Ard Gin Tie Ser Tie Ala Thr Pho Thr Mal Gin Ala Ala Ala Giu
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 <223> Description of Artificial Sequence: Artificial His
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  52.2...
 <221 > 773
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 atg asa bab baa bab baa bat baa bat baa bat baa kat haa
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  42.12 + FRT
  R213 - Mus musculus
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 Met Asp Ala Mot Lys Ar; Gly Lou Cys Tys Val Lou Leu Leu Cys Try
  Ala Val Fhe Val Ser Fro Ser
 <210> 27 <211 + 33
  4212> DNA
  <213 / Homo sapiens
  <221 -
  <221> CDS
  <2222 - (1) ...(33)
  4.40 - 27
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    dlu Glr. Lys Leo Ile Ser Glu Glu Asp Lod Asn
  <2105 28
  <2115 11
  -2105 ERT
  +2195 Homo sapiens
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   3lu 3lm lys Leu 1le Ser 3lu 4lu Asp leu Asm
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Fig. 'B - Various EGF+ isotorms</pre>

4002 34

Val Ser Gin Gln Val Thr Val Gin Ser Ser Pro Asn Phe Thr Gin His 50 55 60

Val Arg Glu Gln Ser Leu Val Thr Asp Gin Leu Ser Arg Arg Leu Fle 65 75 75 80

Arg Thr Tyr Gln Leu Tyr Ser Arg Thr Ser Gly Lys His Val Gln Val

Leu Ala Ash Lys Arg Ile Ash Ala Met Ala Glu Asp Gly Asp Pro Phe 100 105 110

Ala Lys Leu Ile Val Giu Thr Asp Thr Phe Gly Ser Arg Val Arg Val
115 120 125

Arg Gly Ala Glu Thr Gly Leu Ty: The Cys Met Asn Lys Lys Gly Lys 130 140

Leu Ile Ala Lys Ser Ash Gly Lys Gly Lys Asp Cys Val Fhe Thr Glu 145 150 160

The Val Leu Glu Asn Asn Tyr Thr Ala Leu Gln Asn Ala Lys Tyr Glu 165 170 175

Gly Trp Tyr Met Ala Phe Thr Arg Lys Gly Arg Pro Arg Lys Gly Ser 180 185 190

Lys Thr Arg Gln His Gln Arg Glu Val His Phe Met Lys Arg Leu Pro 195 200 205

Arg Gly His His Thr Thr Glu Gln Ser Leu Ary Phe Glu Fhe Leu Ash 210 215 220

Tyr Fro Pro Phe Thr Arg Ser Leu Arg Gly Ser Gln Arg Thr Trp Ala 225 230 235 236 240

Fro Blu Pro Ara

%210% 35 %211% 215 %212 FRT

+21A FRT
+213* Homo sapions

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-221 - mish imathara

+10*+ Pig. * = Wild Typ* WI Fifths

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Armin . The Armin Tyrollin Lau Tyroler Armin Cerolly Tys Els
Ta, din Tal iew Ala Ash iya Arm Ne Ash Ala ibh Ala tib Asp. Hy
Ag Ir The Aladys Let Le Tal Him Thr Asp The He by Ser Arg
The Arg Thi Arg My Alle Ha Thr Gly Led Tyr He Mys Met Ash Dys
lys My Lys Let Tie Ala Lys Ser Ash Gly Lys Bly Lyr Asp Tys Wal
Phy Thr Blu lle Bly Lew Blu Ash Ash Tyr Thr Ala Lew Bin Ash Ala
Lys Tyr Glu Gly Trp Tyr Met Ala Pho Thr Arg Lys Hly Arg Fro Arg
   Gly Ser Lys Thr Arg Gln His Gln Arg Gla Val His Ene Met Lys
Ard Led Fro Arg Gly His His Thr Thr Gld Gln Jer Led Arg Fbe Gld
The Leu Ash Tyr Pro Pro The Thr Arg Ser Leu Ard Sly Ser Him Ard
The Try Ala Pro Glu Pro Ard
+21 36
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5...1. IBT
8015 - Artificial dequence
walls - Fig. 6 - Fs N: Variant of FOF9b with 197 epitigs in the Neterminal
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Mot Ala Bin Val The Val Pho Ash Ash Pho The Val Ser Filo Try Lou
And Mal Fro Lys Mal Ser Ala Cer His Leu Glu Ard Ard Leu Ile Arg
The Tyr Bin Lea Tyr Ser Acr The Ser Bly Lys His Val. His Val. Lea
Ala Ash Lys Ard Ilo Ash Ala Mot Ala Blu Asp Gly Asp Ero The Ala
Tye Ten II. Wal. Min Thr Asy Thr Phe Miy Jer Ard Wal Ard Wal Ard
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lik Ala lye A r Ast. Hy lye Hiy lye Asp Tye Mal His Tim Hit lik
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<2135 Artificial Sequence
<225.
<223> Fig. 6 - F21: Internal variant of FGF8b constructed by replacing
external
      loops in the FGF2 structure with P2 epitope
<400> 37
Met Ala Gin Val Thr Val Gin Ser Ser Fro Ash Fhe Thr Gin His Val
                                    10
Arg Glu Glr. Ser Leu Val Thr Asp Glr Leu Ser Arg Arg Leu 1.0 Arg
            2.0
Thr Tyr Gin Leu Tyr Ser Arg Thr Ser Gly Lys His Val Gin Val Leu
Ala Ash Lys Arg Ile Ash Ala Met Ala Glu Asp Gly Asp Pro Phe Ala
                                            60
Lys Ieu i.c Vai Glu Thr Asp Gln Tyr Ile Lys Ala Ash Ser Lys Phe
                    7.0
65
Tie Gly Nie Thr Blu Leu Gly Ser Arg Val Arg Val Arg Gly Ala Glu
Thr Gly Led Tyr Ile Cys Met Ash Lys Lys Gly Lys Leu Ile Ala Lys
                                105
                                                    110
Ser Asn Gly Lys Gly Lys Asp Cys Val Fhe Thr Glu Ile Gly Leu Glu
Ash Ash Tyr Thr Ala Leu Gln Ash Ala Lys Tyr Glu Gly Trp Tyr Met
Ala Phe The Arg Lys Sly Arg Pro Arg Lys Gly Ser Lys Thr Arg Glm
145
His Glr Ar: Glu Val His Phe Met Tys Ard Leu Pro Arg Gly His His
                165
Thr Throtia Bin Ser Lea Ary Pheotia Pheotea Ash Tyr Protinc Phe
Thr Ard Jer Lea Arg Bly Ser Bln Arg Thr Trp Ala Fro Blu Fre Arg
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Fig. 8. Fig. Prop Fig. 1.
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 Fig. 1.
 Fig. 1.
 Fig. 2.
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Inn Tyn Min teu Tyn Jen Ang Tho Per Sty typ His Mai Gin Mai Les
Ala Ash Lys Arg Ile Ash Ala Met Ala 3. . Asp 3.y Asp Ero Phe Ala
Lys Leu II- Val Siu Thr Asp Thr Phe Siy Jer Arg Val Arg Val Arg
Gly Ala Glu Thr Gly Leu Tyr Ile Cys Met Ash Lys Lys Gly Lys Leu
lle Ala Lys Ger Ash Bly Phe Ash Ash Phe The Val Ser Phe Trp Leu
Arg Val Fro Lys Val Ser Ala Ser His Leu Glu Asp Cys Val Phe Thr
                            120
Glu Ile Gly Leu Glu Asn Asn Tyr Thr Ala Leu Gln Asn Ala Lys Tyr
    130
                        135
Glu Gly Trp Tyr Met Ala Phe Thr Arg Lys Gly Arg Pro Arg Lys Gly
                    150
Ser Lys Thr Arg Gln His Gln Arg Glu Val His Phe Met Lys Arg Leu
                165
Pro Arg Gly His His Thr Thr Glu Glm Ser Leu Arg Phe Glu Phe Leu
            180
                                185
                                                    190
Ash Tyr Fro Pro Phe Thr Arg Ser Leu Arg Sly Ser Gln Arg Thr Trp
        195
                            200
Ala Pro Glu Pro Arg
.210 - 39
<211> 199
<212> PRT
<2135 Artificial Sequence
-2200 ×
<223> Fig. 6 -F20: Variant of FGF9b with 10 epitope in the C-terminal
<4005 39
Met Ala Gli Val Thr Val Gli Ser Ser Fro Asi Fhe Thr Gli His Val
Arg 31: 31: Ser Leu Wal Thr Asp 31: Leu Ser Arg Arg Leu 11e Arg
Thr Tyr Glr. Leu Tyr Ser Ara Thr Ser Gly Lys His Val Glr Val Lou
Ala Ash lys Air ile Ash Ala Met Ala Hu Aug Hly Asp Pro Phe Ala
Lys iso lik Wal. Alo The Asp The Phy. My Ore Are Wal Are Wal Are
My Ala in The Hy Dea Tyr II- dye Met Am Lye Lys Hy Lys Le .
lle Aladys Jer Ast Sty Lys Sty Lys Ast dys Dal Fle Thr Sty Il-
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the Argonic Historia Argonic Valoria Enclided Lyc Arachem Inc. Ara
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iv
Pro Pro Phe The Jin Tyr Ive Lya Ala Ash der Lyo Phe ile Giy ile
Te 180
Thr Blu Lou Fr - Blu Fro Ang
    1 45
×210: 40
<223> A preferred pan DR epitope (FACRE, peptile has this sequence
3400% 41
Ala Lys Fhe Val Ala Ala Trp Thr Let Lys Ala Ala Ala
<2100 41
RATE: ERT
%213* Artitivial Sequence
<220°
<2235 FGF®b specific peptide
<400% 41
Gln Val Thr Val Gln Ser Ser Ero Ash Eng Thr
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